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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,925	09/24/2003	William Hildebrand	66802.055	4622
30589 DUNLAP COD	7590 07/22/200 DDING, P.C.	EXAMINER		
PO BOX 16370			DIBRINO, MARIANNE NMN	
OKLAHOMA CITY, OK 73113			ART UNIT	PAPER NUMBER
			1644	
			MAIL DATE	DELIVERY MODE
			07/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

	Application No.	Applicant(s)			
Office Action Commence	10/669,925	HILDEBRAND ET AL.			
Office Action Summary	Examiner	Art Unit			
	DiBrino Marianne	1644			
The MAILING DATE of this communication app Period for Reply	ears on the cover sheet with the c	orrespondence address			
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION. - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).					
Status					
1) Responsive to communication(s) filed on <u>30 Ar</u>	pril 2008.				
· _ · _ ·	action is non-final.				
·—	/ 				
closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11, 453 O.G. 213.					
Disposition of Claims					
4)⊠ Claim(s) <u>31-42,45,46,48-51,60 and 61</u> is/are pending in the application.					
4a) Of the above claim(s) <u>38-41</u> is/are withdrawn from consideration.					
5) Claim(s) is/are allowed.					
6)⊠ Claim(s) <u>31-37,42,45,46,48-51,60 and 61</u> is/are rejected.					
7) Claim(s) is/are objected to.	•				
8) Claim(s) are subject to restriction and/or	election requirement.				
Application Papers					
9) The specification is objected to by the Examine	r				
10) The drawing(s) filed on is/are: a) accepted or b) objected to by the Examiner.					
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).					
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).					
11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.					
Priority under 35 U.S.C. § 119					
12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).					
a) ☐ All b) ☐ Some * c) ☐ None of:					
1. Certified copies of the priority documents have been received.					
2. Certified copies of the priority documents have been received in Application No					
3. Copies of the certified copies of the priority documents have been received in this National Stage					
application from the International Bureau (PCT Rule 17.2(a)).					
* See the attached detailed Office action for a list of the certified copies not received.					
Attachment(s)					
1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413)					
2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) Information Disclosure Statement(s) (PTO/SB/08)	Paper No(s)/Mail Da 5) Notice of Informal P				
Paper No(s)/Mail Date 6) Other:					

Application/Control Number: 10/669,925

Art Unit: 1644

DETAILED ACTION

Page 2

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/30/08 has been entered.

Applicant's amendment and response filed 4/30/08 is acknowledged and has been entered.

2. Applicant is reminded of Applicant's election of Group I and species of ELISA plate as the substrate, antibody as the anchoring moiety, W6/32 as the antibody, as well as Applicant's election of the species of HLA-A2 with traverse in Applicant's amendment and response filed 12/1/06.

Claims 31-37, 42, 45, 46, 48-51, 60 and 61 are currently being examined.

- 3. The following is a quotation of the first paragraph of 35 U.S.C. 112: The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
- 4. Applicant is reminded that claims 31-37, 42, 45-51, 60 and 61 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendatory material not supported by the disclosure as originally filed is as follows: "at least one MHC trimolecular complex linked thereto" recited in instant base claim 31, "at least one MHC trimolecular complex" recited in claims 35 and in claim 61.

Applicant did not point to support in the disclosure for the claim amendments. Applicant has not addressed this rejection in the amendment and response filed 4/30/08.

Application/Control Number: 10/669,925

Art Unit: 1644

5. Claims 31-37, 42, 45, 46, 48-51, 60 and 61 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Page 3

The amendatory material (in the prior amendment filed 8/20/07) not supported by the disclosure as originally filed is as follows: "wherein the mRNA encodes at least one MHC heavy chain allele" recited in claim 31.

Applicant did not point to support in the disclosure for the claim amendment.

- 6. Applicant's amendment of claim 34 has overcome the 112, 1st paragraph written description and enablement rejections of record in the prior Office Action.
- 7. Applicant's amendment of claim 50 has overcome the 112, 2nd paragraph rejection of record in the prior Office Action.
- 8. For the purpose of prior art rejections, the filing date of the instant claims is deemed to be the filing date of the instant application, *i.e.*, 9/24/03, as the parent applications do not support the claimed limitations of the instant application. The provisional parent application serial no. 60/413,842 only discloses ELISA assays using W6/32 or pan-HLA antibody immobilized HLA to detect anti-HLA antibodies. The provision parent application serial no. 60/474,655 discloses some aspects of making soluble HLA from gDNA or cDNA. The parent application serial no. 10/337,161 and 10/022,066 disclose soluble HLA and making soluble HLA, respectively. In addition, the provisional parent applications do not disclose "pool" and "at least one MHC trimolecular complex" as enunciated at items #4 and #5 supra of this Office Action.
- 9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Application/Control Number: 10/669,925

Art Unit: 1644

10. Claims 31-37, 42, 45, 46, 48-51, 60 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,482, 841 (IDS reference) in view of U.S. Patent No. 5,292,641 (IDS reference), Prilliman *et al* (Immunogenetics. 1997, 45: 379-385, IDS reference), DiBrino *et al* (Biochemistry. 1995, 34(32): 10130-10138, of record) and Zemmour *et al* (J. Immunol. 1992, 148(6): 1941-1948).

Page 4

U.S. Patent No. 5,482, 841 discloses an assay method for detecting the presence of anti-HLA antibodies in a sample, said assay comprising HLA molecules extracted from cells and purified by detergent extraction, centrifugation, PEG and NH₄SO₄ precipitation, said HLA molecules indirectly linked to a solid support such as beads, membranes and microtiter plates by polyclonal or monoclonal antibodies specific for the $\alpha 3$ domain of Class I HLA or the associated \(\beta 2m \) chain or to a conformational epitope expressed by the combination of both chains, or specific to epitopes conserved across a class or subset of HLA molecules, such as ones specific for HLA-A, B or C. U.S. Patent No. 5,482, 841 further discloses that a sample containing antibodies is added, bound antibodies are separated from free antibodies and other non-specifically bound proteins or other components, and the presence of the antibodies is detected using a labeled reagent such as anti-human antibody against IgG, IgM or IgA. U.S. Patent No. 5,482, 841 discloses that the samples may be biological fluids such as blood, CSF, tears, saliva, lymph, dialysis fluid, organ or tissue culture derived fluids and fluids extracted from physiological tissues. U.S. Patent No. 5,482, 841 discloses that of particular interest are allo-antibodies found in the serum of transplant or prospective transplant patients, and that the determination of the presence and specificity of antibodies against foreign HLA antigens is therefore clinically important for monitoring transplant patients, and the assay may test for reactivity against a panel of antigens or may be specific for a single donor. U.S. Patent No. 5,482, 841 discloses that the solid support can be microtiter plates (with wells), glass, plastic, polysaccharides, nylon or nitrocellulose [membranes] or paramagnetic component materials surrounded by plastic. U.S. Patent No. 5,482, 841 discloses using negative and positive control samples. U.S. Patent No. 5,482, 841 discloses a kit for use in a method for detecting at least one receptor analyte specific for an HLA antigen in a biological sample, said kit comprising a solid support coated with a capture agent capable of specifically binding to a conserved region of a subset of interest of HLA antigens and a labeled reagent that specifically binds to human antibodies, and wherein the capture agent may be an antibody directed to the α3 domain of HLA class I heavy chain (see entire reference).

U.S. Patent No. 5,482, 841 does not disclose wherein the pool of HLA molecules is recombinantly produced as recited in the instant claims.

U.S. Patent No. 5,292,641 discloses a kit that includes HLA antigens bound to a solid support, control solutions, and the reagents necessary for the determination of antibodies specific for the HLA antigens (especially column 5 at lines 35-49). U.S. Patent No. 5,292,641 discloses an assay method that utilizes HLA bound to a solid support, said HLA being Class I or Class II or minor histocompatibility antigens and derived from human donors, including from platelets, plasma, serum, lymphoblastoid cell lines, transfectant cell lines, or any other convenient source, said solid support including microtiter plate wells, test tubes, beads, slides, absorbent films, membranes, particles, magnetic particles, glass or plastics. U.S. Patent No. 5,292,641 discloses ELISA techniques and the use of labeled anti-human bodies for detection (see entire reference).

Page 5

Prilliman *et al* teach large-scale production of Class I HLA in roller bottles (*i.e.*, recombinantly produced in a large scale mammalian tissue culture system) for expansion of transfected cells for inoculation into a CELL-PHARM hollow fiber bioreactor for high yield production of Class I HLA. Prilliman *et al* further teach a full-length, single stranded cDNA clone of HLA-B*1501 was used as template in PCR amplification with primers, the 3' primer of which introduces a TGA stop codon, truncating the expressed form of the molecule through removal of the TM and cytoplasmic exons from the coding region. Prilliman *et al* teach the PCR product directionally subcloned into M13, and then subcloned into the mammalian pBJ1-neo expression vector comprising a promoter, and the resulting construct transfected into the class I-negative EBVU-transformed lymphoblastoid line 721.221. The said line was grown in a large-scale culture system and the CELL-PHARM bioreactor, the soluble HLA collected, centrifuged, and subjected to affinity purification processing and fractionation (especially materials and methods section).

DiBrino *et al* teach obtaining and full length cDNA for HLA-B*4403 by PCR amplification of cDNA made from RNA isolated from the immortalized human lymphoblastoid B cell line W1B. The cDNA was sequenced, cloned into the expression vector RSV.neo and transfected into Hmy2.C1R cells (class I deficient cell line). DiBrino *et al* teach detection of said HLA using W6/32 monoclonal antibody specific for human Class I molecules. DiBrino *et al* teach HLA-A2 class I HLA molecules (especially materials and methods section).

Zemmour *et al* teach that Hmy2.C1R cells express HLA-Cw4 as well as reduced levels of HLA-B35 (especially abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have provided recombinantly produced HLA molecules and to have used them in the method for determining anti-HLA antibodies disclosed by U.S. Patent No. 5,482, 841 and U.S. Patent No. 5,292,641. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have produced the soluble HLA molecules by a large-scale production

method taught by Prilliman *et al* using any suitable mammalian cell lines such as the Hmy2.C1R cell line taught by DiBrino *et al* and by Zemmour *et al*, and including the use of W6/32 antibody as a capture agent, and to have included a step of obtaining cDNA encoding class I by reverse transcribing RNA isolated from an immortalized human cell line as taught by DiBrino *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to provide a more easily produced and easily purified source of soluble HLA molecules for use in the method for detecting the presence of anti-HLA antibodies in a sample.

With regard to the limitation "wherein the mammalian cell line expresses endogenous MHC molecules" recited in base claim 31, two references cited in the instant rejection teach the cell line Hmy2.C1R that does express endogenous MHC molecules, and thus the art meets the said claim limitation.

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record in the amendment filed 4/30/08 on pages 12-18.

The Examiner points out that this rejection is a new ground of rejection. The Examiner will address Applicant's arguments that pertain to the instant rejection.

Applicant argues that the fact that the Examiner had to combine teachings from five different references demonstrates that a case of prima facie obviousness has not been established and that hindsight has been used.

In response to Applicant's argument that the Examiner has combined an excessive number of references, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir.1991).

In response to Applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

The '445 patent is not present in the instant rejection. Applicant is arguing the remainder of the references separately.

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir.1986).

Page 7

- 11. Claims 31-37, 42, 45, 46, 48-51, 60 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,482, 841 (IDS reference) in view of U.S. Patent No. 5,292,641 (IDS reference), US 2002/0197672 A1, Prilliman *et al* (Immunogenetics. 1997, 45: 379-385, IDS reference) and DiBrino *et al* (Biochemistry. 1995, 34(32): 10130-10138, of record).
- U.S. Patent No. 5,482, 841 discloses an assay method for detecting the presence of anti-HLA antibodies in a sample, said assay comprising HLA molecules extracted from cells and purified by detergent extraction, centrifugation, PEG and NH₄SO₄ precipitation, said HLA molecules indirectly linked to a solid support such as beads, membranes and microtiter plates by polyclonal or monoclonal antibodies specific for the $\alpha 3$ domain of Class I HLA or the associated \(\beta 2m \) chain or to a conformational epitope expressed by the combination of both chains, or specific to epitopes conserved across a class or subset of HLA molecules, such as ones specific for HLA-A, B or C. U.S. Patent No. 5,482, 841 further discloses that a sample containing antibodies is added, bound antibodies are separated from free antibodies and other non-specifically bound proteins or other components, and the presence of the antibodies is detected using a labeled reagent such as anti-human antibody against IgG, IgM or IgA. U.S. Patent No. 5,482, 841 discloses that the samples may be biological fluids such as blood, CSF, tears, saliva, lymph, dialysis fluid, organ or tissue culture derived fluids and fluids extracted from physiological tissues. U.S. Patent No. 5,482, 841 discloses that of particular interest are allo-antibodies found in the serum of transplant or prospective transplant patients, and that the determination of the presence and specificity of antibodies against foreign HLA antigens is therefore clinically important for monitoring transplant patients, and the assay may test for reactivity against a panel of antigens or may be specific for a single donor. U.S. Patent No. 5,482, 841 discloses that the solid support can be microtiter plates (with wells), glass, plastic, polysaccharides, nylon or nitrocellulose [membrane] or paramagnetic component materials surrounded by plastic. U.S. Patent No. 5,482, 841 discloses using negative and positive control samples. U.S. Patent No. 5,482, 841 discloses a kit for use in a method for detecting at least one receptor analyte specific for an HLA antigen in a biological sample, said kit comprising a solid support coated with a capture agent capable of specifically binding to a conserved region of a subset of interest of HLA antigens and a labeled reagent that specifically binds to human antibodies, and wherein the capture agent may be an antibody directed to the α3 domain of HLA class I heavy chain (see entire reference).
- U.S. Patent No. 5,482, 841 does not disclose wherein the pool of HLA molecules is recombinantly produced as recited in the instant claims.

U.S. Patent No. 5,292,641 discloses a kit that includes HLA antigens bound to a solid support, control solutions, and the reagents necessary for the determination of antibodies specific for the HLA antigens (especially column 5 at lines 35-49). U.S. Patent No. 5,292,641 discloses an assay method that utilizes HLA bound to a solid support, said HLA being Class I or Class II or minor histocompatibility antigens and derived from human donors, including from platelets, plasma, serum, lymphoblastoid cell lines, transfectant cell lines, or any other convenient source, said solid support including microtiter plate wells, test tubes, beads, slides, absorbent films, membranes, particles, magnetic particles, glass or plastics. U.S. Patent No. 5,292,641 discloses ELISA techniques and the use of labeled anti-human bodies for detection (see entire reference).

Page 8

US 2002/0197672 A1 discloses that there has been no readily available source of individual HLA molecules, that the quantities of HLA protein available have been small and typically consists of a mixture of different HLA molecules. US 2002/0197672 A1 further discloses that production of HLA molecules traditionally involves growth and lysis of cells expressing multiple HLA molecules, and to purify native class I or class II molecules from mammalian cells requires time-consuming and cumbersome purification methods. US 2002/0197672 A1 discloses that a need exists in the art for a method of producing substantial quantities of individual HLA class I or class II molecules so that they can be readily purified and isolated independent of other HLA class I or class II molecules; such individual HLA molecules, when provided in sufficient quantity and purity, would provide a powerful tool for studying and measuring immune responses. US 2002/0197672 A1 discloses a method for obtaining cDNA or gDNA encoding a desired MHC class I or class II molecule, PCR amplifying it in a locus-specific manner, producing a truncated form that will be secreted (i.e., lacking the TM and cytoplasmic regions) and that further comprises a tail to facilitate purification, cloning the PCR product into a mammalian expression vector into a mammalian cell line that either lacks or expresses endogenous MHC class I expression (for production of class I), culturing the cell line, and recovering and purifying the soluble MHC molecules. US 2002/0197672 A1 incorporates by reference Prilliman et al, 1997, Immunogenetics, 45: 379-385, see below) which describes establishment of transfectants and culturing cells (especially [0035]-[0036], [0100]).

Prilliman *et al* teach large-scale production of Class I HLA in roller bottles (*i.e.*, recombinantly produced in a large scale mammalian tissue culture system) for expansion of transfected cells for inoculation into a CELL-PHARM hollow fiber bioreactor for high yield production of Class I HLA. Prilliman *et al* further teach a full-length, single stranded cDNA clone of HLA-B*1501 was used as template in PCR amplification with primers, the 3' primer of which introduces a TGA stop codon, truncating the expressed form of the molecule through removal of the TM and cytoplasmic exons from the coding region. Prilliman *et al* teach the PCR product directionally subcloned into M13, and then subcloned into the mammalian pBJ1-neo

expression vector comprising a promoter, and the resulting construct transfected into a mammalian cell line. The said line was grown in a large-scale culture system and the CELL-PHARM bioreactor, the soluble HLA collected, centrifuged, and subjected to affinity purification processing and fractionation, including with an anti- β 2m antibody (especially materials and methods section).

Page 9

DiBrino *et al* teach obtaining and amplifying cDNA for HLA-B*4403 by PCR amplification of cDNA made from RNA isolated from the immortalized human lymphoblastoid B cell line W1B. The cDNA was sequenced, cloned into the expression vector RSV.neo and transfected into Hmy2.C1R cells (class I deficient cell line). DiBrino *et al* teach detection of said HLA using W6/32 monoclonal antibody specific for human Class I molecules. DiBrino *et al* teach HLA-A2 class I HLA molecules (especially materials and methods section).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have provided recombinantly produced HLA molecules and use them in the method disclosed by U.S. Patent No. 5,482, 841. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the method disclosed by US 2002/0197672 A1 for producing large amounts of soluble HLA class I (or class II) molecules in mammalian cells that express endogenous class I (or class II) molecules, and the method including large scale production and purification as taught by Prilliman et al (incorporated by reference into US 2002/0197672 A1), said production including by use of the class I specific antibody W6/32 taught by DiBrino et al and also including the use of W6/32 antibody as a capture agent. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have included a step of obtaining cDNA encoding class I by reverse transcribing RNA isolated from an immortalized human cell line as taught by DiBrino et al. In addition, U.S. Patent No. 5,292,641 discloses another such assay that uses support-bound HLA.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to provide a source of HLA molecules for the method for detecting the presence of anti-HLA antibodies in a sample disclosed by the primary reference U.S. Patent No. 5,482, 841, as US 2002/0197672 A1 discloses that it is advantageous to produce recombinant, soluble HLA molecules rather than isolate them from the surface of cells and discloses a method for doing so, and Prilliman *et al* and DiBrino *et al*, teach methods of isolating, amplifying and large-scale production of specific HLA class I and class II allele products.

Application/Control Number: 10/669,925 Page 10

Art Unit: 1644

Applicant's arguments have been fully considered, but are not persuasive.

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In response to Applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

The '445 patent is not present in the instant rejection. Applicant is arguing the remainder of the references separately.

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir.1986).

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Eileen B. O'Hara, can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Application/Control Number: 10/669,925 Page 11

Art Unit: 1644

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D. Patent Examiner Group 1640 Technology Center 1600 July 11, 2008

/G.R. Ewoldt/ Primary Examiner, Art Unit 1644